REMARKS/ARGUMENTS

Reconsideration and continued examination of the above-identified application are respectfully requested.

Claims 1-2, 5-9, 12-16, 18-28 are pending in the present application. Claims 12-16, 18-19, and 25-27 have been withdrawn from consideration. Claims 3-4, 10-11, and 17 are canceled. By way of this amendment, claims 1, 2, 5-9, and 20-21 have been amended as explained below. The limitations of claim 3 are essentially encompassed by amended claims 1, 20, and 21, therefore, claim 3 has been canceled. Support for these amendments can be found throughout the present application, including pages 24 and 43 of the present application. Therefore, no new questions of patentability should arise nor does the amendment necessitate any further searching on the part of the Examiner. The amendment places the application in condition for allowance. At a minimum, the amendment places the application in a better condition for appeal. Accordingly, no questions of new matter should arise and entry of this amendment is respectfully requested.

Interview Summary

The applicants and applicants' representative appreciate the courtesies extended to the applicants' representative by the Examiner during the telephone interview held on February 25, 2008. During the interview, applicants' representative discussed how the claimed invention was distinct from the constructs described in Pavlinkova et al. Amendments to claims 1, 20 and 21 were also discussed.

Rejection of claims 2-9 under 35 U.S.C. §112, second paragraph

At page 6 of the Office Action, the Examiner states that the rejection of claims 2-9 for the

recitation that the antibody "carries" or is "carrying" a labeling substance in the linker part is maintained.

The Examiner also states that the rejection of claim 9 is maintained for the recitation that the antibody "has a Kd value that is equivalent to a Kd value of a naturally occurring antibody" is maintained. The rejections are respectfully traversed.

The language objected to by the Examiner, though clear to one skilled in the art, has been removed. Accordingly, this rejection should be withdrawn.

Rejection of claims 3, 4, 7, 8, 20-24, and 28 under 35 U.S.C. §112, second paragraph

At page 7 of the Office Action, the Examiner states that claims 3, 4, 7, 8, 20-24, and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner states that claims 3, 4, 7, 8, 20-24, and 28 are indefinite for the recitation "labeling substance is a substance that is capable of binding to a polypeptide of the linker part of the antibody in the presence of a specific enzyme." The Examiner states that it is not clear what the relationship is between the labeling substance that is bound to the linker and the polypeptide that is part of the linker. The Examiner states that claim 20 is indefinite for the recitation "wherein DNA is subjected to transcription and translation utilizing a wheat embryo-derived cell-free protein translation system in the presence of a labeling substance and an enzyme that catalyzes a disulfide bond exchange reaction." The Examiner states that it is not clear how the labeling substance and the enzyme that catalyzes a disulfide bond exchange reaction contribute to the transcription and translation of the DNA in the wheat embryo-derived cell-free protein. The Examiner further states that claim 20 is indefinite for the recitation "the DNA encoding the linker comprises a nucleotide sequence that is capable of binding with a labeling substance in the presence of a specific enzyme after translation."

The Examiner states that it is not clear how the nucleotide sequence binds the labeling substance in the presence of the enzyme. This rejection is respectfully traversed.

In order to further clarify the relationship between the labeling substance, the linker, and the enzyme recited in the claims, the phrase "in the presence of a specific enzyme" in claims 3, 4, 7, 8, 20-24, and 28 has been replaced with the phrase "wherein the linker comprises an amino acid sequence that can be recognized by an enzyme that is capable of binding the labeling substance to the linker." The phrase "wherein the DNA encoding a linker comprises a nucleotide sequence that is capable of binding with a labeling substance in the presence of a specific enzyme after translation" has also been deleted. Accordingly, these aspects of the rejection are rendered moot.

Claim 20 has further been amended to recite utilizing a wheat embryo-derived cell-free protein translation system in the presence of a labeling substance and in the presence of an enzyme that catalyzes a disulfide-bond exchange reaction, to further clarify that the enzyme catalyzes a disulfide bond exchange reaction, not the labeling substance. As discussed in the present application, by carrying out a translation reaction in which an enzyme that catalyzes a disulfide bond exchange reaction is further added to a weak reductive translation reaction solution, it is possible to conduct highly efficient synthesis of a protein that retains an intramolecular bond (page 30).

Accordingly, this rejection should be withdrawn.

Priority Filing Date

At page 8 of the Office Action, the Examiner states that the priority filing date of JP 2002-210067 (filed 7/18/2002) has not been acknowledged because a certified translation of priority document has not been filed.

According to 37 C.F.R. 1.55, an English language translation of a non-English language foreign application is not required except when the application is involved in an interference, when it is necessary to overcome the date of a reference relied upon by the Examiner, or when specifically required by the Examiner. As none of the conditions set forth in 37 C.F.R. § 1.55 for providing an English language translation are present in the instant case, a certified English translation of the Japanese priority document should not be required to establish the Japanese priority date.

Rejection of claims 1, 2, 5, 6, 21, 23, and 24 under 35 U.S.C. §102(a) – Pavlinkova et al

Beginning at page 8 of the Office Action and continuing to page 10, the Examiner states that claims 1, 2, 5, 6, 21, 23, and 24 are rejected under 35 U.S.C. §102(a) as being anticipated by Pavlinkova et al. (Peptides 24:353-362 (March, 2003)). The Examiner states that Pavlinkova et al. discloses scFv antibodies having peptide linkers and streptavidin-binding peptide or a biotin-link mimetic peptide (BMP), where the scFV is modified to contain the BMP. The Examiner states that Pavlinkova et al. discloses that the BMP can be added to the carboxyl terminus of the VH region. The Examiner reasons that the dimeric scFv would require that the BMP bind to the linker vis-à-vis fusion (see Office Action, pages 9-10). The Examiner states that insertion of a biotin-like or BMP labeling substance within the linker or binding to the linker vis-à-vis fusion was already known in the art. This rejection is respectfully traversed.

The presently claimed invention is different from Pavlinkova et al. Claim 1 explicitly recites that the heavy and light chain of the antibody are directly crosslinked through a linker and that the linker is bound to a labeling substance. Pavlinkova et al. does not teach or suggest a linker that is bound to a labeling substance and directly crosslinks the heavy and light chains of an

antibody. In fact, the teachings of Pavlinkova et al. are contrary to the teachings of the present application. Pavlinkova et al. states that BMP is added to the carboxyl terminus of the heavy chain of the antibody (page 354, col. 2, para. 2). As stated in the present application, however, the activity of an antibody to bind with an antigen is reduced when a label, such as biotin, is bound to the C-terminus or N-terminus of the antibody, as opposed to a linker (page 2, lines 1-8; page 3, lines 15-26).

If it could somehow be assumed that the BMP described in Pavlinkova et al. binds to the linker and the carboxyl terminus of the VH region, as suggested by the Examiner in the Office Action, the linker in Pavlinkova et al. is still distinguished from the linker recited in the present claims because Pavlinkova et al. does not indicate that the linker would in that case, also directly cross-link the heavy and light chain domains.

In order to assist the Examiner, however, claims 1, 20, and 21 further recite that the linker comprises an amino acid sequence that can be recognized by an enzyme that is capable of binding the labeling substance to the linker. Pavlinkova et al. does not teach or suggest a linker having an amino acid sequence that can be recognized by an enzyme that is capable of binding a labeling substance to a linker. It should also be noted that this limitation essentially corresponds to and further clarifies the recitation in claim 3 that the labeling substance is "capable of binding to a polypeptide of the linker part of the antibody in the presence of a specific enzyme." As this reference was not cited against claim 3, it is respectfully submitted that claims 1, 20, and 21, as amended, also distinguish over Pavlinkova et al. for this additional reason.

Accordingly, this rejection should be withdrawn.

Rejection of claims 1, 9, 21, and 28 under 35 U.S.C. §103(a) -- Pavlinkova et al. in view of Fricker et al.

Beginning at page 10 of the Office Action and continuing to page 13, the Examiner states that claims 1, 9, 21, and 28 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pavlinkova et al. in view of Fricker et al. (U.S. Patent Application Publication No. 2004/0265902). The Examiner acknowledges that Pavlinkova et al. does not disclose production in a wheat-embryo derived cell-free translation system. The Examiner states that one skilled in the art would have readily modified the scFv of Pavlinkova et al. to have been expressed in a wheat-embryo derived system in order to obtain a homogenous, exogenous protein free scFv isolate. This rejection is respectfully traversed.

The differences between the claimed invention and Pavlinkova et al. stated above apply equally here. Further, Fricker et al. does not teach or suggest a linker that directly cross-links heavy and light chain domains of antibody and that is bound to a labeling substance, as recited in the present claims. Fricker et al. also fails to teach or suggest a linker having an amino acid sequence that can be recognized by an enzyme that is capable of binding a labeling substance to a linker. As such, Fricker et al. fails to overcome the deficiencies in Pavlinkova et al.

Accordingly, this rejection should be withdrawn.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request the reconsideration of this application and the timely allowance of the pending claims.

If there are any other fees due in connection with the filing of this response, please charge the fees to Deposit Account No. 50-0925. If a fee is required for an extension of time under 37

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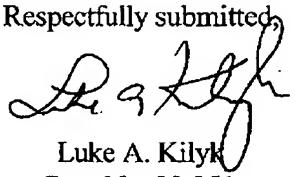
C.F.R. § 1.136 not accounted for above, such extension is requested and should also be charged to said Deposit Account.

Respectfully submitted,



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